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Book Review

Genetics and Tuberculosis

NOVARTIS FOUNDATION SYMPOSIUM 217 Chichester: John Wiley & Sons, Chadwick DJ, Cardew G, eds: 1998; 269 pages. £75·00. ISBN 0-471-98261 X.

When one picks up a book entitled Genetics and Tuberculosis, one opens the front cover with anticipation. After more than a century of extensive research, one is confronted with how little we know about tuberculosis and how much of that missing knowledge must be within the topic which the title identifies. The fact that, on average, only a minority of those extensively exposed to the bacillus become infected; that only a minority of those infected develop disease; that many who develop disease are cured even if they do not receive treatment. Not only this, but the wide variation in probability of each of these transitions and the fact that the bacillus may lie 'dormant' for years and even decades before causing the disease remain tantalizing indicators of the complexity of this disease. This complexity must be, at least in part, explained by the genetics of the pathogen and of the host.

Sections of the book most relevant to this discussion include the following: host genetic susceptibility to human tuberculosis, page 3; cellular and genetic mechanisms underlying susceptibility of animal models to tuberculosis infection, page 112; susceptibility to tuberculosis as a complex genetic trait, page 120; analysis of the genome of *Mycobacterium tuberculosis* H37Rv, page 160 and Bacterial genetics and strain variation, page 190. The former three would be expected to deal with the host genetics and the latter that of the agent.

The first set of papers, while touching on aspects of the host genetics relevant to the host–agent interaction, gives little solid data but reflects on methods which may be particularly rewarding in studying human genetics and its influence on response to tubercle bacilli. The second section deals, as its title suggests, primarily with animal models, although it also reflects on the relevance of the animal models to human disease. In this section, the author suggests that the mouse model may be helpful in particular in indicating the genetic basis of reactivation. The early response to the bacillus leading to innate versus acquired immune response may predict the likelihood of subsequent reactivation of the bacilli in the human. The third section, again, reflects on genetic aspects of susceptibility indicated in mouse models of tuberculosis. In this section, the authors posit the utility of a particular model, using the recombinant congenic strain of mice, in unraveling the complex host response to the bacillus. These sections, taken together, indicate how little we understand the human genetic aspects of tuberculosis, although they do outline progress that has been made recently in the study of laboratory animals as models of this disease.

The second set of papers deals with the genetics of the agent. The first paper in this set outlines the remarkable achievement of characterization of the genome of *Mycobacterium tuberculosis*. This has been truly a momentous achievement in the fight against tuberculosis and in the understanding of the disease. The paper describes aspects of the sequencing and goes on to discuss anitgenic variability of the agent which might underlie varying study results which have been obtained under similar circumstances in different locations. The second paper in this group outlines the genetic patterns and their significance for the epidemic within communities. It discusses the significance of what is known at present and indicates what is not known. It goes on to place this knowledge into a theoretical framework of the bacillus and its development, transmission and persistence within the community.

The book contains other sections that deal with immunopathogenesis of tuberculosis as follows: immunological and endocrinological characteristics of tuberculosis that provide opportunities for immunotherapeutic intervention, page 73 and signals that regulate the host response to *Mycobacterium tuberculosis*, page 157. Many of the remaining sections deal with the practical consequences of genetic techniques in our study of tuberculosis and the methods for its control.

Having started out with anticipation, what is our mood when we have finished reading this book? Clearly, the subject remains an area of study of great, and we must say, vital importance if we to make progress in tackling tuberculosis. Very important progress has been made in the genetics of the agent, although this progress is just now beginning to provide information on which we can begin to revise our understanding of the disease. In spite of its importance, we must conclude that progress in understanding the host response has lagged behind even though it will undoubtedly be at least as important, and likely more important to our understanding of this disease.

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